## SEQUENCE LISTING

## (1) GENERAL INFORMATION:

- (i) APPLICANT: Markussen, Jan Jonassen, Ib Havelund, Svend Brandt, Jakob Kurtzhals, Peter Hansen, Hertz Per
- (ii) TITLE OF INVENTION: INSULIN DERIVATIVES
- (iii) NUMBER OF SEQUENCES: 26
- (iv) CORRESPONDENCE ADDRESS:
  - (A) ADDRESSEE: Novo Nordisk of North America, Inc.
  - (B) STREET: 405 Lexington Avenue, 64th Floor

  - (C) CITY: New York (D) STATE: New York
  - (E) COUNTRY: United States of America
  - (F) ZIP: 10174-6401
- (v) COMPUTER READABLE FORM:
  - (A) MEDIUM TYPE: Floppy disk
  - (B) COMPUTER: IBM PC compatible
  - (C) OPERATING SYSTEM: PC-DOS/MS-DOS
  - (D) SOFTWARE: PatentIn Release #1.0, Version #1.30
- (vi) CURRENT APPLICATION DATA:
  - (A) APPLICATION NUMBER: to be assigned
  - (B) FILING DATE: 17-SEPT-1997
  - (C) CLASSIFICATION:
- (viii) ATTORNEY/AGENT INFORMATION:
  - (A) NAME: Lambiris, Elias J.

  - (B) REGISTRATION NUMBER: 33,728
    (C) REFERENCE/DOCKET NUMBER: 4341.204-US
  - (ix) TELECOMMUNICATION INFORMATION:
    - (A) TELEPHONE: 212-867-0123 (B) TELEFAX: 212-878-9655
- (2) INFORMATION FOR SEQ ID NO:1:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 21 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:
  - Gly Ile Val Glu Gln Cys Cys Thr Ser Ile Cys Ser Leu Tyr Gln Leu
  - Glu Asn Tyr Cys Xaa
- (2) INFORMATION FOR SEQ ID NO:2:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 30 amino acids
    - (B) TYPE: amino acid

- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Xaa Xaa Xaa Gln His Leu Cys Gly Ser His Leu Val Glu Ala Leu Tyr

Leu Val Cys Gly Glu Arg Gly Phe Phe Xaa Xaa Xaa Xaa Xaa 20 25

- (2) INFORMATION FOR SEQ ID NO:3:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 5 amino acids

    - (B) TYPE: amino acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

Tyr Thr Pro Lys Thr

- (2) INFORMATION FOR SEQ ID NO:4:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 5 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Tyr Thr Pro Lys Ala

- (2) INFORMATION FOR SEQ ID NO:5:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 5 amino acids

    - (B) TYPE: amino acid (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

Ser Asp Asp Ala Arg

- (2) INFORMATION FOR SEQ ID NO:6:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 13 amino acids

    - (B) TYPE: amino acid (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

Glu Glu Ala Glu Ala Glu Pro Lys Ala Thr Arg

	(1)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 5 amino acids  (B) TYPE: amino acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:7:	
	Ser 1	Asp Asp Ala Arg	,
(2)	INFO	RMATION FOR SEQ ID NO:8:	
	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 7 amino acids (B) TYPE: amino acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:8:	·
	Thr 1	Lys Ser Asp Asp Ala Arg 5	•
(2)	INFO	RMATION FOR SEQ ID NO:9:	
	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 6 amino acids (B) TYPE: amino acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:9:	
	Lys 1	Ser Asp Asp Ala Arg 5	
(2)	INFO	RMATION FOR SEQ ID NO:10:	
	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 112 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:10:	
CCA	AGTAC	AA AGCTTCAACC AAGTGGGAAC CGCACAAGTG TTGGTTAACG AATCTTGTAG	60
CCT:	TTGGTT	IC AGCTTCAGCT TCAGCTTCTT CTCTTTTATC CAAAGAAACA CC	112
(2)	INFO	RMATION FOR SEQ ID NO:11:	
	(i)	SEQUENCE CHARACTERISTICS:  (A) LENGTH: 27 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear	
	(xi)	SEQUENCE DESCRIPTION: SEQ ID NO:11:	

(2) INFORMATION FOR SEQ ID NO:7:

TAAATCTATA ACTACAAAAA ACACATA	27
(2) INFORMATION FOR SEQ ID NO:12:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 79 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:	
TTGGTTGAAG CTTTGTACTT GGTTTGCGGT GAAAGAGGTT TCTTCTACAC TCCTAAGTCT	60
GACGATGCTA GAGGTATTG	79
(2) INFORMATION FOR SEQ ID NO:13:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 27 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:	
TTAATCTTAG TTTCTAGAGC CTGCGGG	27
(2) INFORMATION FOR SEQ ID NO:14:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 85 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:	
TTGGTTGAAG CTTTGTACTT GGTTTGCGGT GAAAGAGGTT TCTTCTACAC TCCTACCAAG	60
TCTGACGATG CTAGAGGTAT TGTCG	85
(2) INFORMATION FOR SEQ ID NO:15:	
<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 71 base pairs</li> <li>(B) TYPE: nucleic acid</li> <li>(C) STRANDEDNESS: single</li> <li>(D) TOPOLOGY: linear</li> </ul>	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:	
CACTTGGTTG AAGCTTTGTA CTTGGTTTGC GGTGAAAGAG GTTTCTTCTA CACTAAGTCT	60
GACGATGCTA G	71
(2) INFORMATION FOR SEQ ID NO:16:	
<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 68 base pairs</li> <li>(B) TYPE: nucleic acid</li> <li>(C) STRANDEDNESS: single</li> </ul>	

## (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO:16: CACTTGGTTG AAGCTTTGTA CTTGGTTTGC GGTGAAAGAG GTTTCTTCTA CAAGTCTGAC 60 **GATGCTAG** 68 (2) INFORMATION FOR SEQ ID NO:17: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 66 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: single (D) TOPOLOGY: linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO:17: CACTTGGTTG AAGCTTTGTA CTTGGTTTGC GGTGAAAGAG GTTTCTTCAA AGTCTGACGA 60 TGCTAG 66 (2) INFORMATION FOR SEQ ID NO:18: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 594 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double (D) TOPOLOGY: linear (ix) FEATURE: (A) NAME/KEY: CDS (B) LOCATION: 109..522 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:18: CTTAAATCTA TAACTACAAA AAACACATAC AGGAATTCCA TTCAAGAATA GTTCAAACAA 60 GAAGATTACA AACTATCAAT TTCATACACA ATATAAACGA TTAAAAGA ATG AGA TTT Met Arg Phe 1 CCT TCT ATT TTT ACT GCT GTT TTA TTC GCT GCT TCC GCT TTA GCT Pro Ser Ile Phe Thr Ala Val Leu Phe Ala Ala Ser Ser Ala Leu Ala 165 10 GCT CCA GTC AAC ACT ACC ACT GAA GAT GAA ACG GCT CAA ATT CCA GCT 213 Ala Pro Val Asn Thr Thr Glu Asp Glu Thr Ala Gln Ile Pro Ala 25 30 GAA GCT GTC ATC GGT TAC TCT GAT TTA GAA GGT GAT TTC GAT GTT GCT 261 Glu Ala Val Ile Gly Tyr Ser Asp Leu Glu Gly Asp Phe Asp Val Ala GTT TTG CCA TTT TCC AAC TCC ACC AAT AAC GGT TTA TTG TTT ATC AAT 309 Val Leu Pro Phe Ser Asn Ser Thr Asn Asn Gly Leu Leu Phe Ile Asn 55 ACT ACT ATT GCC TCC ATT GCT GCT AAA GAA GAA GGT GTT TCT TTG GAT Thr Thr Ile Ala Ser Ile Ala Ala Lys Glu Glu Gly Val Ser Leu Asp 357 AAA AGA TTC GTT AAC CAA CAC TTG TGC GGT TCC CAC TTG GTT GAA GCT 405 Lys Arg Phe Val Asn Gln His Leu Cys Gly Ser His Leu Val Glu Ala

90

GCT Ala	AAG Lys	GGI	' ATT	GTC Val	Glu	CAA Gln	TGC	TGT Cys	ACC Thr 125	Ser	ATC Ile	TGC Cys	TCC Ser	TTG Leu 130	Tyr
CAA Gln	TTG Leu	GAA Glu	AAC Asn 135	Tyr	TGC Cys	AAC Asn	TAG	ACGC	AGC	CCGC	AGGC	TC T	AGAA	ACTA	A
GAT	TAAT	ATA	ATTA	TATA -	AA A	ATAT	TATC	т тс	TTTT	CTTT	AТ				
(2)	INF	ORMA	TION	FOR	SEQ	ID :	NO:1	9:							
		(i)	(B	ENCE ) LE ) TY ) TO	NGTH PE:	: 13	8 am o ac	ino id		s					
	(	ii)	MOLE	CULE	TYP	E: p	rote	in							
	(:	xi)	SEQU.	ENCE	DES	CRIP'	rion	: SE	Q ID	NO:	19:				
Met 1	Arg	Phe	Pro	Ser 5	Ile	Phe	Thr	Ala	Val 10	Leu	Phe	Ala	Ala	Ser 15	Ser
Ala	Leu	Ala	Ala 20	Pro	Val	Asn	Thr	Thr 25	Thr	Glu	Asp	Glu	Thr 30	Ala	Gln
Ile	Pro	Ala 35	Glu	Ala	Val	Ile	Gly 40	Tyr	Ser	Asp	Leu	Glu 45	Gly	Asp	Phe
Asp	Val 50	Ala	Val	Leu	Pro	Phe 55	Ser	Asn	Ser	Thr	Asn 60	Asn	Gly	Leu	Leu
Phe 65	Ile	Asn	Thr	Thr	Ile 70	Ala	Ser	Ile	Ala	Ala 75	Lys	Glu	Glu	Gly	Val 80
Ser	Leu	Asp	Lys	Arg 85	Phe	Val	Asn	Gln	His 90	Leu	Cys	Gly	Ser	His 95	Leu
Val	Glu	Ala	Leu 100	Tyr	Leu	Val	Cys	Gly 105	Glu	Arg	Gly	Phe	Phe 110	Tyr	Thr
Pro	Lys	Ala 115	Ala	Lys	Gly	Ile	Val 120	Glu	Gln	Cys	Cys	Thr 125	Ser	Ile	Cys
Ser	Leu 130	Tyr	Gln	Leu	Glu	Asn 135	Tyr	Суз	Asn					٠	
(2)	INFO	RMAI	CION	FOR	SEQ	ID N	iO:20	) :							

TTG TAC TTG GTT TGC GGT GAA AGA GGT TTC TTC TAC ACT CCT AAG GCT Leu Tyr Leu Val Cys Gly Glu Arg Gly Phe Phe Tyr Thr Pro Lys Ala 100

453

501

552

594

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 4 amino acids
    (B) TYPE: amino acid
    (C) STRANDEDNESS: single
    (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: None

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

Thr Gly Gly Lys

- (2) INFORMATION FOR SEQ ID NO:21:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 4 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: None
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

Thr Glu Gly Lys

- (2) INFORMATION FOR SEQ ID NO:22:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 4 amino acids
      (B) TYPE: amino acid

    - (C) STRANDEDNESS: single (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: None
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

Gly Asp Thr Lys

- (2) INFORMATION FOR SEQ ID NO:23:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 8 amino acids
      (B) TYPE: amino acid

    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: None
  - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

Gly Thr Lys Ser Asp Asp Ala Arg

- (2) INFORMATION FOR SEQ ID NO:24:
  - (i) SEQUENCE CHARACTERISTICS:
    - (A) LENGTH: 7 amino acids
    - (B) TYPE: amino acid
    - (C) STRANDEDNESS: single
    - (D) TOPOLOGY: linear
  - (ii) MOLECULE TYPE: None

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:	
Gly Lys Ser Asp Asp Ala Arg 1 5	
(2) INFORMATION FOR SEQ ID NO:25:	
(i) SEQUENCE CHARACTERISTICS:  (A) LENGTH: 85 base pairs  (B) TYPE: nucleic acid  (C) STRANDEDNESS: single  (D) TOPOLOGY: linear	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:	
TTGGTTGAAG CTTTGTACTT GGTTTGCGGT GAAAGAGGTT TCTTCTACAC TGGTACCAAG TCTGACGATG CTAGAGGTAT TGTCG	6 8
(2) INFORMATION FOR SEQ ID NO:26:	
<ul> <li>(i) SEQUENCE CHARACTERISTICS:</li> <li>(A) LENGTH: 82 base pairs</li> <li>(B) TYPE: nucleic acid</li> <li>(C) STRANDEDNESS: single</li> <li>(D) TOPOLOGY: linear</li> </ul>	
(ii) MOLECULE TYPE: CDNA	
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:	
TTGGTTGAAG CTTTGTACTT GGTTTGCGGT GAAAGAGGTT TCTTCTACAC CGGTAAGTCT GACGATGCTA GAGGTATTGT CG	6 9 8 :